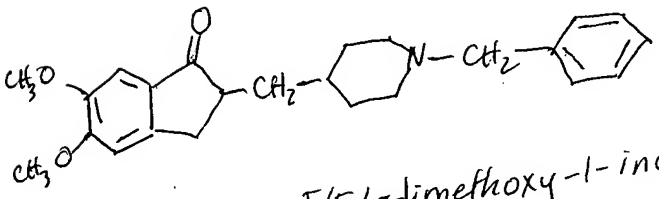
10/726,486

EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	3627	((514/317) or (514/319) or (514/315)).CCLS.	US-PGPUB; USPAT; USOCR	OR	OFF	2006/11/20 11:11
L2	406	((544/195) or (544/192)).CCLS.	US-PGPUB; USPAT; USOCR	OR	OFF	2006/11/20 11:12
L3	2298	L1 or L2	USPAT	OR	OFF	2006/11/20 11:12
L4	103	L3 and (indane or indanon or indanone)	USPAT	OR	OFF	2006/11/20 11:12

Refs of Yokoyama (US 2006/0172992 & US 2006/0135507) teach the same cmpd for opposite use (treating overactive bladder).



±1-benzyl-4-[(5,6-dimethoxy-1-indanon)-2-yl]methylpiperidine

AKA: "Donepezil" or ARICEPT

Related US Pats: 6900683, 6455544, 6482838, 6413986, 5100901, 5985864, 6140321

All teach Donepezil for treating attention disorder or cognitive impairment.

10/ 726,486

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NEWS 5	AUG 30	CA(SM)/CAplus(SM) Austrian patent law changes
NEWS 6	SEP 11	CA/CAplus enhanced with more pre-1907 records
NEWS 7	SEP 21	CA/CAplus fields enhanced with simultaneous left and right truncation
NEWS 8	SEP 25	CA(SM)/CAplus(SM) display of CA Lexicon enhanced
NEWS 9	SEP 25	CAS REGISTRY(SM) no longer includes Concord 3D coordinates
NEWS 10	SEP 25	CAS REGISTRY(SM) updated with amino acid codes for pyrrolysine
NEWS 11	SEP 28	CEABA-VTB classification code fields reloaded with new classification scheme
NEWS 12	OCT 19	LOGOFF HOLD duration extended to 120 minutes
NEWS 13	OCT 19	E-mail format enhanced
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NEWS 15	OCT 23	CAS Registry Number crossover limit increased to 300,000 in multiple databases
NEWS 16	OCT 23	The Derwent World Patents Index suite of databases on STN has been enhanced and reloaded
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NEWS 18	NOV 03	JAPIO enhanced with IPC 8 features and functionality
NEWS 19	NOV 10	CA/CAplus F-Term thesaurus enhanced
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NEWS 21	NOV 13	CA/CAplus pre-1967 chemical substance index entries enhanced with preparation role

NEWS EXPRESS NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8
NEWS X25	X.25 communication option no longer available

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FILE 'HOME' ENTERED AT 11:02:04 ON 20 NOV 2006

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 11:02:16 ON 20 NOV 2006

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 19 NOV 2006 HIGHEST RN 913611-00-4
DICTIONARY FILE UPDATES: 19 NOV 2006 HIGHEST RN 913611-00-4

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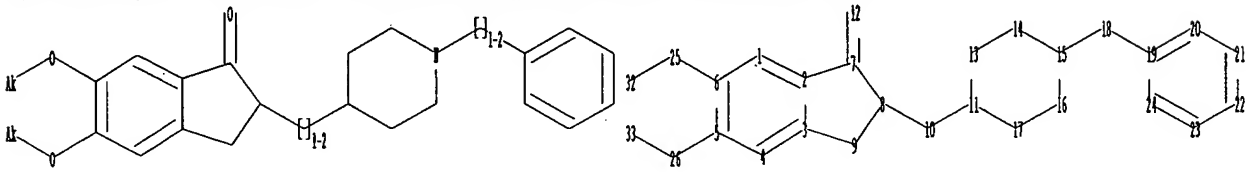
REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=>
Uploading C:\Program Files\Stnexp\Queries\10726486a.str



chain nodes :
10 12 18 25 26 32 33
ring nodes :
1 2 3 4 5 6 7 8 9 11 13 14 15 16 17 19 20 21 22 23 24
chain bonds :
5-26 6-25 7-12 8-10 10-11 15-18 18-19 25-32 26-33
ring bonds :
1-2 1-6 2-3 2-7 3-4 3-9 4-5 5-6 7-8 8-9 11-13 11-17 13-14 14-15 15-16 16-17 19-20 19-24 20-21 21-22 22-23 23-24
exact/norm bonds :
5-26 6-25 7-12 15-18 25-32 26-33
exact bonds :
2-7 3-9 7-8 8-9 8-10 10-11 11-13 11-17 13-14 14-15 15-16 16-17 18-19
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 19-20 19-24 20-21 21-22 22-23 23-24
isolated ring systems :
containing 1 : 11 : 19 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:CLASS
11:Atom 12:CLASS 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:CLASS 19:Atom
20:Atom 21:Atom 22:Atom 23:Atom 24:Atom 25:CLASS 26:CLASS 32:CLASS 33:CLASS

L1 STRUCTURE UPLOADED

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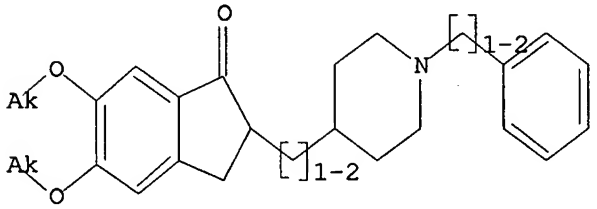
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

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SAMPLE SEARCH INITIATED 11:02:40 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 12 TO ITERATE

100.0% PROCESSED 12 ITERATIONS 9 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 33 TO 447
PROJECTED ANSWERS: 9 TO 360

L2 9 SEA SSS SAM L1

=> s l1 ful
FULL SEARCH INITIATED 11:03:12 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 284 TO ITERATE

100.0% PROCESSED 284 ITERATIONS 228 ANSWERS
SEARCH TIME: 00.00.01

L3 228 SEA SSS FUL L1

=> file hcaplus
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 167.38 167.59

FILE 'HCAPLUS' ENTERED AT 11:03:30 ON 20 NOV 2006
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FILE COVERS 1907 - 20 Nov 2006 VOL 145 ISS 22
FILE LAST UPDATED: 19 Nov 2006 (20061119/ED)

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This file contains CAS Registry Numbers for easy and accurate
substance identification.

```
=> s l3
L4          933 L3

=> s L4 and (urina? or bladder or excretory or dysuria)
         129021 URINA?
          35027 BLADDER
           6221 EXCRETORY
            267 DYSURIA
L5           30 L4 AND (URINA? OR BLADDER OR EXCRETORY OR DYSURIA)

=> d his

     (FILE 'HOME' ENTERED AT 11:02:04 ON 20 NOV 2006)

     FILE 'REGISTRY' ENTERED AT 11:02:16 ON 20 NOV 2006
L1               STRUCTURE UPLOADED
L2             9 S L1 SAMPLE
L3           228 S L1 FUL

     FILE 'HCAPLUS' ENTERED AT 11:03:30 ON 20 NOV 2006
L4           933 S L3
L5            30 S L4 AND (URINA? OR BLADDER OR EXCRETORY OR DYSURIA)

=> d l5 1- ibib abs hitstr
YOU HAVE REQUESTED DATA FROM 30 ANSWERS - CONTINUE? Y/(N):y
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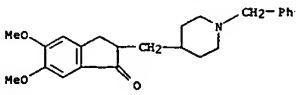
L5 ANSWER 1 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:990012 HCAPLUS
DOCUMENT NUMBER: 145:410513
TITLE: Acetylcholinesterase inhibitor acting on the brain improves detrusor overactivity caused by cerebral infarction in rats
AUTHOR(S): Nakai, M.; Akino, H.; Kaneda, T.; Matsuta, Y.; Shiyama, R.; Tanase, K.; Ito, H.; Aoki, Y.; Oyama, N.; Miwa, Y.; Yokoyama, O.
CORPORATE SOURCE: Department of Urology, University of Fukui, Matsuoka, Fukui, Japan
SOURCE: Neuroscience (San Diego, CA, United States) (2006), 142(2), 475-480
CODEN: NRSCDN; ISSN: 0306-4522
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Purpose: The functional contribution of the cholinergic pathway in the frontal cortex to micturition was evaluated following cerebral ischemia. Furthermore, it was examined whether reactivation of this regulatory system using acetylcholinesterase inhibitor could improve detrusor overactivity. Methods: Left middle cerebral artery occlusion (MCAO) was performed in female Sprague-Dawley rats. Choline acetyltransferase (ChAT) activities after MCAO were assayed to assess the damage to cholinergic neurons. ChAT activities in the bilateral cortex, hippocampus, and pons were calculated by measuring the conversion of 1-[14C] acetyl-CoA to [14C] acetylcholine. Effects on cystometrog. of i.v. or i.c.v. donepezil hydrochloride (DON), a centrally acting acetylcholinesterase inhibitor, were investigated in conscious sham-operated (SO) and cerebral infarcted (CI) rats. To investigate whether DON in the forebrain was affected, we decerebrated rats after CI or SO, and investigated the effects on cystometrog. of i.v. DON. Results: Bladder capacity was markedly decreased after MCAO, and remained below half of the pre-occlusion capacity. The greatest increase in bladder capacity was attained at 1.2 + 10-2 nM/kg of DON given i.v., with a change of 52.8% (P<0.05). In cases of i.c.v. DON, the greatest increase in bladder capacity was at the dose of 6 + 10-2 pmol with the change of 95.8% (P<0.01). The activity of ChAT was decreased in the left cortex and hippocampus 24 h after MCAO (P<0.05). In decerebrated rats, low dose of DON did not change micturition parameters. Conclusions: These results suggest that by upregulation of the forebrain muscarinic inhibitory mechanism, acetylcholinesterase inhibitor improves detrusor overactivity by cerebral infarction.

IT 120011-70-3, Donepezil hydrochloride
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(acetylcholinesterase inhibitor acting on brain improves detrusor overactivity caused by cerebral infarction)
RN 120011-70-3 HCAPLUS
CN 1H-Inden-1-one, 2,3-dihydro-5,6-dimethoxy-2-[[1-(phenylmethyl)-4-piperidinyl]methyl]-, hydrochloride (9CI) (CA INDEX NAME)

L5 ANSWER 1 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



● HCl

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

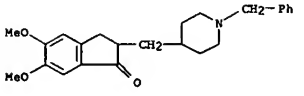
L5 ANSWER 2 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:817760 HCAPLUS
DOCUMENT NUMBER: 145:180983
TITLE: Treating microvasculature diseases with acetylcholinesterase inhibitors
INVENTOR(S): Wills, Stephen
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 61pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2006086698	A2	20060817	WO 2006-US4857		20060210
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
US 2006183733	A1	20060817	US 2006-352165		20060210
PRIORITY APPLN. INFO.:			US 2005-651613P	P	20050211
			US 2005-663204P	P	20050321
			US 2005-670256P	P	20050412
			US 2005-677366P	P	20050504

AB There is disclosed a method of treating various diseases caused by micro-vasculature circulation problems, including, but not limited to, vascular insufficiency, phantom pain, diabetic neuropathy, neuropathic pain, autoimmune/inflammatory diseases (e.g., multiple sclerosis, Parkinson's disease, Crohn's Disease, lupus, rheumatoid arthritis, polymyalgia rheumatica, polymyositis, dermatomyositis, sarcoidosis), urinary retention, lymphoedema, and chronic renal insufficiency. Specifically, there is disclosed a treatment providing an effective amount of an acetyl cholinesterase inhibitor compound (or combination of compds.) to treat one or a plurality of microvasculature diseases.

IT 120011-70-3, Aricept
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treating microvasculature diseases with acetylcholinesterase inhibitors)
RN 120011-70-3 HCAPLUS
CN 1H-Inden-1-one, 2,3-dihydro-5,6-dimethoxy-2-[[1-(phenylmethyl)-4-piperidinyl]methyl]-, hydrochloride (9CI) (CA INDEX NAME)

L5 ANSWER 2 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



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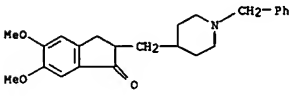
L5 ANSWER 3 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:769191 HCAPLUS
DOCUMENT NUMBER: 145:202921
TITLE: Therapeutic agent for overactive bladder resulting from cerebral infarction
INVENTOR(S): Yokoyama, Osamu; Nakai, Masaharu
PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan
SOURCE: U.S. Pat. Appl. Publ., 40pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006172992	A1	20060803	US 2005-203901	20050815
PRIORITY APPLN. INFO.:			US 2004-601425P P	20040813

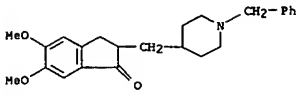
OTHER SOURCE(S): MARPAT 145:202921
AB An agent for treating overactive bladder resulting from cerebral infarction, comprising administering a compound having a cholinesterase inhibitory activity or a pharmacol. acceptable salt thereof.
IT 120011-70-3P, Donepezil Hydrochloride
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(therapeutic agent for overactive bladder resulting from cerebral infarction)
RN 120011-70-3 HCAPLUS
CN 1H-Inden-1-one, 2,3-dihydro-5,6-dimethoxy-2-[[1-(phenylmethyl)-4-piperidinyl]methyl]-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

IT 120014-06-4 120014-11-1 120014-13-3
120014-15-5
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapeutic agent for overactive bladder resulting from cerebral infarction)
RN 120014-06-4 HCAPLUS
CN 1H-Inden-1-one, 2,3-dihydro-5,6-dimethoxy-2-[[1-(phenylmethyl)-4-piperidinyl]methyl]- (9CI) (CA INDEX NAME)

L5 ANSWER 3 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 120014-11-1 HCAPLUS
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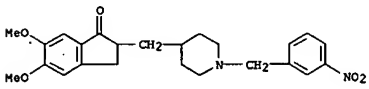
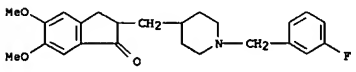
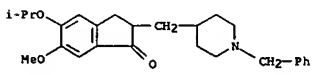


RN 120014-13-3 HCAPLUS
CN 1H-Inden-1-one, 2-[[1-[(3-fluorophenyl)methyl]-4-piperidinyl]methyl]-2,3-dihydro-5,6-dimethoxy- (9CI) (CA INDEX NAME)

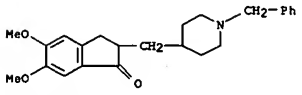


RN 120014-15-5 HCAPLUS
CN 1H-Inden-1-one, 2,3-dihydro-6-methoxy-5-(1-methylethoxy)-2-[[1-(phenylmethyl)-4-piperidinyl]methyl]- (9CI) (CA INDEX NAME)



L5 ANSWER 4 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:438288 HCAPLUS
DOCUMENT NUMBER: 145:389101
TITLE: 3-Year Study of Donepezil Therapy in Alzheimer's Disease: Effects of Early and Continuous Therapy
AUTHOR(S): Winblad, B.; Wimo, A.; Engedal, K.; Soininen, H.; Verhey, F.; Waldemar, G.; Wetterholm, A.-L.; Haglund, A.; Zhang, R.; Schindler, R.
CORPORATE SOURCE: Donepezil Nordic Study Group, Karolinska University Hospital Huddinge, Stockholm, Swed.
SOURCE: Dementia and Geriatric Cognitive Disorders (2006), 21(5-6), 353-363
CODEN: DGCDFX; ISSN: 1420-8008
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Delays in the diagnosis of Alzheimer's disease, and, therefore, delays in treatment, may have a detrimental effect on a patient's long-term well-being. This study assessed the effects of postponing donepezil treatment for 1 yr by comparing patients treated continuously for 3 years with those who received placebo for 1 yr followed by open-label donepezil for 2 years. Patients (n = 286) with possible or probable Alzheimer's disease (according to DSM-IV, NINCDS-ADRDA, and Mini-Mental State Examination
criteria; see text) were randomized to receive donepezil (5 mg/day for 4 wk, 10 mg/day thereafter) or placebo (delayed-start group) for 1 yr. Of the 192 completers, 157 began a 2-yr, open-label phase of donepezil treatment. Outcome measures were the Gottfries-Brane-Steen scale, the Mini-Mental State Examination, the Global Deterioration Scale, the Progressive
Deterioration Scale, the Neuropsychiatric Inventory, and safety (adverse events). Mixed regression anal. was used to compare changes between the groups over 3 years on the efficacy measures. There was a trend for patients receiving continuous therapy to have less global deterioration (Gottfries-Brane-Steen scale) than those who had delayed treatment (p = 0.056). Small but statistically significant differences between the groups were observed for the secondary measures of cognitive function (Mini-Mental State Examination; p=0.004) and cognitive and functional abilities
(Global Deterioration Scale; p = 0.0231) in favor of continuous donepezil therapy. Over 90% of the patients in both cohorts experienced one treatment-emergent adverse event; most were considered mild or moderate. In conclusion, patients in whom the start of treatment is delayed may demonstrate slightly reduced benefits as compared with those seen in patients starting donepezil therapy early in the course of Alzheimer's disease. These data support the long-term efficacy and safety of donepezil.
IT 120014-06-4, Donepezil
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(long term donepezil therapy was well tolerated and that incidence of Alzheimer's disease decreases in patient over time with treatment)
RN 120014-06-4 HCAPLUS
CN 1H-Inden-1-one, 2,3-dihydro-5,6-dimethoxy-2-[[1-(phenylmethyl)-4-piperidinyl]methyl]- (9CI) (CA INDEX NAME)

L5 ANSWER 4 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)

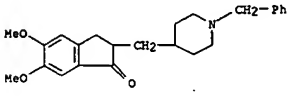


REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 5 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:268371 HCAPLUS
DOCUMENT NUMBER: 144:305160
TITLE: Therapeutic drugs for age-related overactive bladder containing cholinesterase inhibitors, treatment of overactive bladder with the drugs, and screening of the drugs
INVENTOR(S): Yokoyama, Osamu; Nakai, Shoji; Akino, Hironobu
PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 44 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

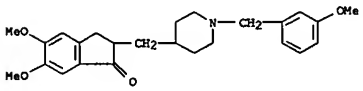
PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
JP 2006077006	A2	20060323	JP 2005-235436		20050815
US 2006135507	A1	20060622	US 2005-203899		20050815
PRIORITY APPLN. INFO.:			JP 2004-235932	A	20040813
			US 2004-601442P	P	20040813

OTHER SOURCE(S): MARPAT 144:305160
AB The drugs contain cholinesterase inhibitors, their pharmacol.-acceptable salts, or solvates thereof. The inhibitors may be cyclic amine derivs. (Markush structures given). Substances which inhibit age-related overactive bladder are screened by (1) administering cholinesterase-inhibiting compds., their salts, or solvates thereof to nonhuman mammals and (2) detecting or measuring ≥1 change selected from those in bladder volume, bladder contraction pressure, and residual urine volume Thus, i.v. administration of donepezil hydrochloride (preparation given) to rats having vesical fistula increased bladder volume
IT 120011-70-3P, Donepezil hydrochloride
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cholinesterase inhibitors for treatment of age-related overactive bladder and drug screening using change in bladder volume, bladder contraction pressure, or residual urine volume as index)
RN 120011-70-3 HCAPLUS
CN 1H-Inden-1-one, 2,3-dihydro-5,6-dimethoxy-2-[[1-(phenylmethyl)-4-piperidinyl]methyl]-, hydrochloride (9CI) (CA INDEX NAME)



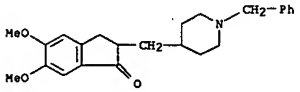
● HCl

L5 ANSWER 5 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)

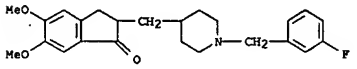


L5 ANSWER 5 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)

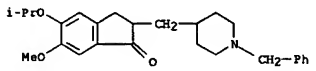
IT 120014-06-4 120014-13-3 120014-15-5
361547-23-1
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cholinesterase inhibitors for treatment of age-related overactive bladder and drug screening using change in bladder volume, bladder contraction pressure, or residual urine volume as index)
RN 120014-06-4 HCAPLUS
CN 1H-Inden-1-one, 2,3-dihydro-5,6-dimethoxy-2-[[1-(phenylmethyl)-4-piperidinyl]methyl]- (9CI) (CA INDEX NAME)



RN 120014-13-3 HCAPLUS
CN 1H-Inden-1-one, 2-[[1-[(3-fluorophenyl)methyl]-4-piperidinyl]methyl]-2,3-dihydro-5,6-dimethoxy- (9CI) (CA INDEX NAME)



RN 120014-15-5 HCAPLUS
CN 1H-Inden-1-one, 2,3-dihydro-6-methoxy-5-(1-methylethoxy)-2-[[1-(phenylmethyl)-4-piperidinyl]methyl]- (9CI) (CA INDEX NAME)

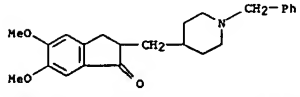


RN 361547-23-1 HCAPLUS
CN 1H-Inden-1-one, 2,3-dihydro-5,6-dimethoxy-2-[[1-[(3-methoxyphenyl)methyl]-4-piperidinyl]methyl]- (9CI) (CA INDEX NAME)

L5 ANSWER 6 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:151208 HCAPLUS
DOCUMENT NUMBER: 144:219324
TITLE: Transnasal composition having immediate action and high absorbability
INVENTOR(S): Nagata, Ryoichi; Haruta, Shunji
PATENT ASSIGNEE(S): Translational Research, Ltd., Japan
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006016530	A1	20060216	WO 2005-JP14389	20050805
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
PRIORITY APPLN. INFO.:			JP 2004-233660	A 20040810

AB Disclosed is a powdery composition for transnasal administration which contains a nonpeptidic nonproteinaceous drug and crystalline cellulose masses having a specific mesh-size as a carrier therefor. This composition can exert an immediate action of the drug and a high absorbability. For example, morphine hydrochloride 65 mg and Avicel PH-F20 (crystalline cellulose) 135 mg were blended and nasally administered to monkeys for the determination of pharmacokinetic parameters of morphine.
IT 120014-06-4, Donepezil
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(transnasal powder composition having immediate action and high absorbability)
RN 120014-06-4 HCAPLUS
CN 1H-Inden-1-one, 2,3-dihydro-5,6-dimethoxy-2-[[1-(phenylmethyl)-4-piperidinyl]methyl]- (9CI) (CA INDEX NAME)

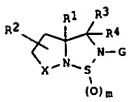


REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 7 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:904349 HCAPLUS
DOCUMENT NUMBER: 143:248278
TITLE: Preparation of sulfonylpyrrolidines as modulators of androgen receptor
INVENTOR(S): Hamann, Lawrence G.; Bi, Yingzhi; Manfredi, Mark C.; Nirschl, Alexandra A.; Sutton, James C.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 35 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005187267	A1	20050825	US 2005-48439	20050201
PRIORITY APPLN. INFO.:			US 2004-541869P P	20040204
OTHER SOURCE(S):	MARPAT 143:248278			

GI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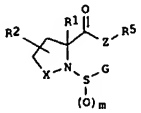
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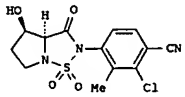
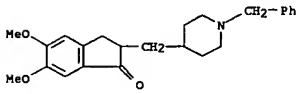

III

AB Title compds. I or II [R1 = H, (un)substituted alkyl, alkenyl, etc.; R2 = H, halo, SR6, etc.; R3 and R4 independently = H, (un)substituted alkynyl, cycloalkyl, etc.; R5 = H, (un)substituted aryl, arylalkyl, etc.; R6 = H, CHF2, CF3, etc.; X = (CH2)n; G = (un)substituted aryl, heterocycle or heteroaryl; Z = O or NR7; R7 = H, (un)substituted alkyl, alkenyl, etc.; n and m independently = 1-2] and their pharmaceutically acceptable salts, are prepared and disclosed as modulators of androgen receptor. Thus, e.g.,

L5 ANSWER 7 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)
III was prepd. by hydrolysis of (2S,3R)-1-(3-chloro-4-cyano-2-methylphenylsulfamoyl)-3-hydroxy-pyrrolidine-2-carboxylic acid Me ester (prepn. given) followed by cyclization. The activity of I was evaluated in transactivation assays of a transfected reporter construct and using the endogenous androgen receptor of the host cells (no data). I as modulator of androgen receptor should prove useful in the treatment of neoplasm, Alzheimer's disease and obesity. Pharmaceutical compns. comprising I are disclosed.
IT 120014-06-4
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(claimed co-drug; preparation of sulfonylpyrrolidines as modulators of androgen receptor)
RN 120014-06-4 HCAPLUS
CN 1H-Inden-1-one, 2,3-dihydro-5,6-dimethoxy-2-[[1-(phenylmethyl)-4-piperidinyl]methyl]- (9CI) (CA INDEX NAME)



L5 ANSWER 8 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:902874 HCAPLUS
DOCUMENT NUMBER: 143:248277
TITLE: Preparation of sulfonylpyrrolidines as modulators of androgen receptor
INVENTOR(S): Hamann, Lawrence H.; Bi, Yingzhi; Manfredi, Mark C.; Nirschl, Alexandra A.; Sutton, James C.
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 91 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005077925	A1	20050825	WO 2005-US2834	20050202
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1718626	A1	20061108	EP 2005-712320	20050202
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, TR, BG, CZ, EE, HU, PL, SK, HR, IS, YU				
PRIORITY APPLN. INFO.:			US 2004-541869P P	20040204
			WO 2005-US2834 W	20050202
OTHER SOURCE(S):	MARPAT 143:248277			

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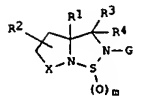
L5 ANSWER 8 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)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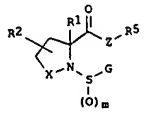
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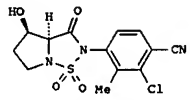
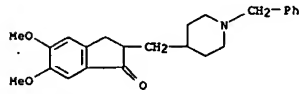

III

AB Title compds. I or II [R1 = H, (un)substituted alkyl, alkenyl, etc.; R2 = H, halo, SR6, etc.; R3 and R4 independently = H, (un)substituted alkynyl, cycloalkyl, etc.; R5 = H, (un)substituted aryl, arylalkyl, etc.; R6 = H, CHF2, CF3, etc.; X = (CH2)n; G = (un)substituted aryl, heterocycle or heteroaryl; Z = O or NR7; R7 = H, (un)substituted alkyl, alkenyl, etc.; n and m independently = 1-2] and their pharmaceutically acceptable salts, are prepared and disclosed as modulators of androgen receptor. Thus, e.g., III was prepared by hydrolysis of (2S,3R)-1-(3-chloro-4-cyano-2-methylphenylsulfamoyl)-3-hydroxy-pyrrolidine-2-carboxylic acid Me ester (preparation
given) followed by cyclization. The activity of I was evaluated in transactivation assays of a transfected reporter construct and using the endogenous androgen receptor of the host cells (no data). I as modulator of androgen receptor should prove useful in the treatment of neoplasm, Alzheimer's disease and obesity. Pharmaceutical compns. comprising I are disclosed.
IT 120014-06-4, Donepezil
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(claimed co-drug; preparation of sulfonylpyrrolidines as modulators of androgen receptor)
RN 120014-06-4 HCAPLUS
CN 1H-Inden-1-one, 2,3-dihydro-5,6-dimethoxy-2-[[1-(phenylmethyl)-4-piperidinyl]methyl]- (9CI) (CA INDEX NAME)



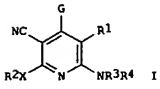
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS

L5 ANSWER 8 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 9 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:824492 HCAPLUS
DOCUMENT NUMBER: 143:222525
TITLE: Method of using 3-cyano-4-arylpyridine derivatives as modulators of androgen receptor function, preparation thereof, and use with other agents
INVENTOR(S): Nirschl, Alexandra A.; Hamann, Lawrence G.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 25 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2005182105	A1	20050818	US 2005-48437		20050201
PRIORITY APPLN. INFO.:			US 2004-541780P	P	20040204

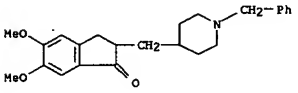
OTHER SOURCE(S): MARPAT 143:222525
GI



AB A method is provided for treating androgen receptor-associated conditions, such as age-related diseases, e.g. sarcopenia, employing a compound I [R1 = CN, H; X = O, S; R2 = (substituted) alkyl, (substituted) cycloalkyl, etc; R3, R4 = H, (substituted) alkyl, etc.; G = (substituted) aryl, (substituted) heteroaryl], or a pharmaceutically acceptable salt or prodrug ester thereof. Preparation of selected I is described. I may be used in combination with other agents.

IT 120014-06-4, Donepezil
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyanoarylpyridine derivative modulators of androgen receptor function, preparation, and use with other agents)

RN 120014-06-4 HCAPLUS
CN 1H-Inden-1-one, 2,3-dihydro-5,6-dimethoxy-2-[[1-(phenylmethyl)-4-piperidinyl]methyl]- (9CI) (CA INDEX NAME)



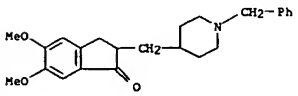
L5 ANSWER 9 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)

L5 ANSWER 10 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:498931 HCAPLUS
DOCUMENT NUMBER: 143:126558
TITLE: Urodynamic assessment of donepezil hydrochloride in patients with Alzheimer's disease
AUTHOR(S): Sakakibara, Ryuji; Uchiyama, Tomoyuki; Yoshiyama, Mitsuharu; Yamanishi, Tomoyuki; Hattori, Takamichi
CORPORATE SOURCE: Department of Neurology, Chiba University, Chiba, Japan
SOURCE: Neurourology and Urodynamics (2005), 24(3), 273-275
CODEN: NEUREM; ISSN: 0733-2467
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Donepezil hydrochloride, a central cholinergic drug, is widely used for improving cognitive decline in Alzheimer's disease (AD). We investigated whether donepezil might affect the lower urinary tract (LUT) function in AD. Alzheimer's Disease Assessment Scale cognitive subscale (ADAS-cog) (0-70, increase as impairment), urinary questionnaire, and electromyog. (EMG)-cystometry were performed in eight patients with AD before and after treatment with 5 mg/day of donepezil. The first assessment (before donepezil) showed moderate cognitive decline in the patients as a mean ADAS-cog score of 27.0 (range: 17-35) (normal <15). Seven patients had urinary symptoms including urinary urgency incontinence in five. EMG-cystometry revealed neurogenic detrusor overactivity in seven with a mean detrusor pressure of 44.9 cmH2O (20-101), mean bladder capacity of 202 mL (20-412), and post-void residuals in none. The second assessment (3 mo after donepezil) showed a decrease in the ADAS-cog score to 23.3 (11-35) though without statistical significance. Urinary incontinence disappeared in one and none had a new onset of incontinence. EMG-cystometry revealed an increase in the detrusor pressure on overactivity to 54.1 cmH2O (20-122), but also an increase in the bladder capacity to 234 mL (80-400), and post-void residuals in one (40 mL). Although the number of our patients was small, it seems possibly that donepezil could ameliorate cognitive function without serious adverse effects on the LUT function in patients with AD.

IT 120011-70-3, Donepezil hydrochloride
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(donepezil hydrochloride ameliorated cognitive function without serious adverse effects on lower urinary tract function in Alzheimer's disease patient)

RN 120011-70-3 HCAPLUS
CN 1H-Inden-1-one, 2,3-dihydro-5,6-dimethoxy-2-[[1-(phenylmethyl)-4-piperidinyl]methyl]-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS

L5 ANSWER 10 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 11 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:324165 HCAPLUS
DOCUMENT NUMBER: 142:392284
TITLE: Preparation of indole derivatives as COX-1-, COX-2-, and β-catenin-inhibitors
INVENTOR(S): Chao, Qi; Elliott, Gary T.; Leoni, Lorenzo; Phillips, Mimi K.
PATENT ASSIGNEE(S): Salmedix, Inc., USA
SOURCE: PCT Int. Appl., 141 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005033113	A2	20050414	WO 2004-US32185	20041001
WO 2005033113	A3	20050630		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2540343	AA	20050414	CA 2004-2540343	20041001
EP 1673373	A2	20060628	EP 2004-793917	20041001
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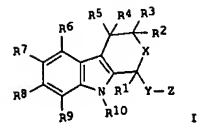
PRIORITY APPLN. INFO.:
US 2003-508592P P 20031002
US 2004-556599P P 20040326
WO 2004-US32185 W 20041001

OTHER SOURCE(S): MARPAT 142:392284
GI

L5 ANSWER 11 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



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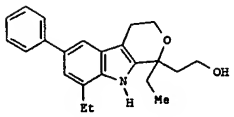


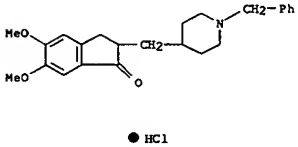
II

AB Title compds. I [X = C, S, O; R1 = H, halo, OH, etc.; R2, R3, R4, and R5 independently = H, SH, CN, etc.; R6, R7, R8, and R9 independently = H, NO2, CN, etc.; R10 = H, (un)substituted-alkyl, -alkenyl, etc.; Y = (un)substituted-alkyl, -alkenyl, -alkynyl, etc.; Z = OH, SH, SO2NH2, etc.; R1 and Y may cyclize to (un)substituted-cycloalkyl or -heterocycloalkyl group] and their pharmaceutically acceptable salts, are prepared and disclosed as inhibitors of COX-1, COX-2, and β-catenin. Thus, e.g., II was prepared by reduction of (5-bromo-7-ethyl-1H-indol-3-yl)-oxo-acetic acid Et ester (preparation given) followed by condensation with Et propionylacetate and subsequent reduction/Suzuki coupling. The cell cytotoxicity of I was evaluated and revealed that selected compds. of the invention possessed LNCap IC50 values in the range of 3-235 nm. I should prove useful in the treatment of diseases such as, but not limited to, lung cancer, diabetes and Alzheimer's disease.

IT 120011-70-3, Donepezil hydrochloride
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(claimed co-drug; preparation of indole derivs. as COX-1-, COX-2-, and β-catenin-inhibitors)

RN 120011-70-3 HCAPLUS
CN 1H-Inden-1-one, 2,3-dihydro-5,6-dimethoxy-2-[[1-(phenylmethyl)-4-piperidinyl]methyl]-, hydrochloride (9CI) (CA INDEX NAME)

L5 ANSWER 11 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



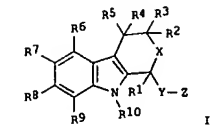
● HCl

L5 ANSWER 12 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

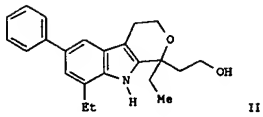
ACCESSION NUMBER: 2005:324164 HCAPLUS
DOCUMENT NUMBER: 142:373682
TITLE: Preparation of indole derivatives as COX-1-, COX-2-, and β-catenin-inhibitors
INVENTOR(S): Chao, Qi; Elliott, Gary T.; Leoni, Lorenzo
PATENT ASSIGNEE(S): Salmedix, Inc., USA
SOURCE: PCT Int. Appl., 143 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005033112	A2	20050414	WO 2004-US32184	20041001
WO 2005033112	A3	20050609		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2540289	AA	20050414	CA 2004-2540289	20041001
EP 1680428	A2	20060719	EP 2004-809825	20041001
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
PRIORITY APPLN. INFO.:			US 2003-508592P	P 20031002
			US 2004-556599P	P 20040326
			WO 2004-US32184	W 20041001

OTHER SOURCE(S): MARPAT 142:373682
GI



I



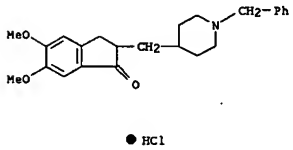
II

AB Title compds. I [X = C, S, O; R1 = H, halo, OH, etc.; R2, R3, R4, and R5 independently = H, SH, CN, etc.; R6, R7, R8, and R9 independently = H, NO2, CN, etc.; R10 = H, (un)substituted-alkyl, -alkenyl, etc.; Y = (un)substituted-alkyl, -alkenyl, -alkynyl, etc.; Z = OH, SH, SO2NH2, etc.; R1 and Y may cyclize to (un)substituted-cycloalkyl or -heterocycloalkyl group] and their pharmaceutically acceptable salts, are prepared and disclosed as inhibitors of COX-1, COX-2, and β-catenin. Thus, e.g., II was prepared by reduction of (5-bromo-7-ethyl-1H-indol-3-yl)-oxo-acetic acid Et ester (preparation given) followed by condensation with Et propionylacetate and subsequent reduction/Suzuki coupling. The cell cytotoxicity of I was evaluated and revealed that selected compds. of the invention possessed LNCap IC50 values in the range of 3-235 nm. I should prove useful in the treatment of diseases such as, but not limited to, lung cancer, diabetes and Alzheimer's disease.

IT 120011-70-3, Donepezil hydrochloride
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(claimed co-drug; preparation of indole derivs. as COX-1-, COX-2-, and β-catenin-inhibitors)

RN 120011-70-3 HCAPLUS
CN 1H-Inden-1-one, 2,3-dihydro-5,6-dimethoxy-2-[[1-(phenylmethyl)-4-piperidinyl]methyl]-, hydrochloride (9CI) (CA INDEX NAME)

L5 ANSWER 12 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



● HCl

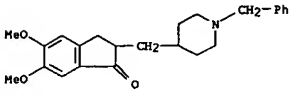
L5 ANSWER 13 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:565091 HCAPLUS
DOCUMENT NUMBER: 141:99726
TITLE: Therapeutic formulations for the treatment of beta-amyloid related diseases containing two active ingredients
INVENTOR(S): Gervais, Francine; Bellini, Francesco
PATENT ASSIGNEE(S): Neurochem International Limited, Switz.
SOURCE: PCT Int. Appl., 179 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 10
PATENT INFORMATION:

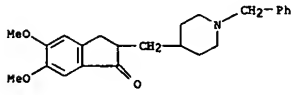
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004058258	A1	20040715	WO 2003-CA2011	20031224
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2511606	AA	20040715	CA 2003-2511606	20031224
AU 2003291910	A1	20040722	AU 2003-291910	20031224
EP 1585520	A1	20051019	EP 2003-767368	20031224
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003017747	A	20051122	BR 2003-17747	20031224
CN 1753662	A	20060329	CN 2003-80109946	20031224
CN 1753675	A	20060329	CN 2003-80109952	20031224
JP 2006512417	T2	20060413	JP 2005-509679	20031224
US 2005031651	A1	20050210	US 2004-871537	20040618
NO 2005003077	A	20050922	NO 2005-3077	20050623
PRIORITY APPLN. INFO.:			US 2002-436379P	P 20021224
			US 2003-482214P	P 20030623
			US 2003-480906P	P 20030623
			US 2003-480918P	P 20030623
			US 2003-480984P	P 20030623
			US 2003-482058P	P 20030623
			US 2003-512017P	P 20031017
			US 2003-512047P	P 20031017
			US 2003-512116P	P 20031017
			US 2003-512135P	P 20031017
			US 2003-746138	A2 20031224
			WO 2003-CA2011	W 20031224

OTHER SOURCE(S): MARPAT 141:99726
AB This invention relates to methods and pharmaceutical compns. for treating amyloid-β related diseases, including Alzheimer's disease. The invention, for example, includes a method of concomitant therapeutic treatment of a subject, comprising administering an effective amount of a first agent and a second agent, wherein said first agent treats an amyloid-β disease, neurodegeneration, or cellular toxicity; and said second agent is a therapeutic drug or nutritive supplement. Pharmaceutical compns. containing compds. of the invention and a kit containing

L5 ANSWER 13 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)
pharmaceutical formulations of the invention are also claimed.
IT 120014-06-4, Donepezil
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapeutic formulations for treatment of beta-amyloid related diseases containing two active ingredients)
RN 120014-06-4 HCAPLUS
CN 1H-Inden-1-one, 2,3-dihydro-5,6-dimethoxy-2-[[1-(phenylmethyl)-4-piperidinyl]methyl]- (9CI) (CA INDEX NAME)



L5 ANSWER 14 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)
administering to a mammal in need thereof a therapeutically effective amt. of a compd. of the invention. Compd. prepn. is included.
IT 120014-06-4, Donepezil
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(p-hydroxymilnacipran stereoisomers, therapeutic use, and use with other agents)
RN 120014-06-4 HCAPLUS
CN 1H-Inden-1-one, 2,3-dihydro-5,6-dimethoxy-2-[[1-(phenylmethyl)-4-piperidinyl]methyl]- (9CI) (CA INDEX NAME)



L5 ANSWER 14 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:392439 HCAPLUS
DOCUMENT NUMBER: 140:400095
TITLE: Stereoisomers of p-hydroxy-milnacipran, and therapeutic use
INVENTOR(S): Rariy, Roman V.; Heffernan, Michael; Buchwald, Stephen L.; Swager, Timothy M.
PATENT ASSIGNEE(S): Collegium Pharmaceutical, Inc., USA
SOURCE: PCT Int. Appl., 163 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004039320	A2	20040513	WO 2003-US33681	20031022
WO 2004039320	A3	20040624		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2503381	AA	20040513	CA 2003-2503381	20031022
AU 2003284342	A1	20040525	AU 2003-284342	20031022
US 2004142904	A1	20040722	US 2003-691465	20031022
US 7038085	B2	20060502		
EP 1578719	A2	20050928	EP 2003-776524	20031022
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006503920	T2	20060202	JP 2005-501895	20031022

PRIORITY APPLN. INFO.:
US 2002-421640P P 20021025
US 2002-423062P P 20021101
US 2003-445142P P 20030205
WO 2003-US33681 W 20031022

OTHER SOURCE(S): MARPAT 140:400095
AB The invention relates generally to the enantiomers of p-hydroxymilnacipran or congeners thereof. Biol. assays revealed that racemic p-hydroxymilnacipran is approx. equipotent in inhibiting serotonin and norepinephrine uptake (IC50 = 28.6 nM for norepinephrine, IC50 = 21.7 nM for serotonin). Interestingly, (+)-p-hydroxymilnacipran is a more potent inhibitor of norepinephrine uptake than serotonin uptake (IC50 = 10.3 nM for norepinephrine, IC50 = 22 nM for serotonin). In contrast, (-)-p-hydroxymilnacipran is a more potent inhibitor of serotonin uptake compared to norepinephrine uptake (IC50 = 88.5 nM for norepinephrine, IC50 = 40.3 nM for serotonin). The invention also relates to salts and prodrug forms of the above compds. In certain embodiments, the compds. of the invention and a pharmaceutically acceptable excipient are combined to prepare a formulation for administration to a patient. Finally, the invention relates to methods of treating mammals suffering from various afflictions, e.g., depression, chronic pain, or fibromyalgia, comprising

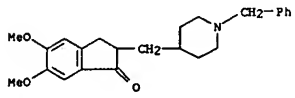
L5 ANSWER 15 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:354723 HCAPLUS
DOCUMENT NUMBER: 140:368732
TITLE: Methods and compositions using cholinesterase inhibitors for the treatment of nervous system disorders and other conditions
INVENTOR(S): Ieni, John; Pratt, Raymond
PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004034963	A2	20040429	WO 2003-US15279	20030516
WO 2004034963	A3	20040722		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003298514	A1	20040504	AU 2003-298514	20030516
US 2006018839	A1	20060126	US 2004-988600	20041116

PRIORITY APPLN. INFO.:
US 2002-380852P P 20020517
US 2003-447724P P 20030219
WO 2003-US15279 W 20030516

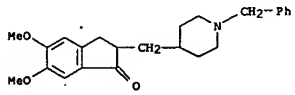
OTHER SOURCE(S): MARPAT 140:368732
AB The invention provides methods for treating and/or preventing Alzheimer's disease, psychiatric illnesses, encephalitis, meningitis, fetal alc. syndrome, Korsakoff's syndrome, anoxic brain injury, cardiopulmonary resuscitation injuries, diabetes, Sjogren's syndrome, mental retardation, developmental delay, menopause, strokes, macular degeneration, neuronal loss associated with macular degeneration, sleep disorders, severe Alzheimer's disease, jet lag, post-traumatic stress disorder, anxiety disorders, panic attacks, obsessive-compulsive disorder, amnesia, and other disorders by administering to a patient in need thereof at least one cholinesterase inhibitor. The invention also provides novel pharmaceutical compns. that can be administered to the eyes or to the nose of patients. In one embodiment, the cholinesterase inhibitor is donepezil, a stereoisomer thereof and/or a pharmaceutically acceptable salt thereof. In other embodiments, the cholinesterase inhibitor can be one or more of phenserine, tolserine, phenethylnorcymserine, ganstigmine, epastigmine, tacrine, physostigmine, pyridostigmine, neostigmine, rivastigmine, galantamine, citicoline, velnacrine, huperzine, metrifonate, heptastigmine, edrophonium, TAK-147, T-82, and upreazine.
IT 120011-70-3 120014-06-4, Donepezil 120014-09-7
120014-11-1 120014-13-3 120014-15-5
142057-80-5 142698-19-9
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cholinesterase inhibitors for treatment of nervous system disorders and other conditions, and pharmaceutical compns.)
RN 120011-70-3 HCAPLUS

L5 ANSWER 15 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)
CN 1H-Inden-1-one, 2,3-dihydro-5,6-dimethoxy-2-[[1-(phenylmethyl)-4-piperidinyl]methyl]-, hydrochloride (9CI) (CA INDEX NAME)

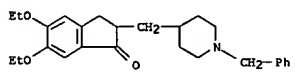


● HCl

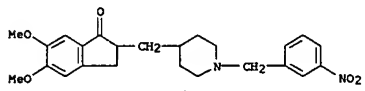
RN 120014-06-4 HCAPLUS
CN 1H-Inden-1-one, 2,3-dihydro-5,6-dimethoxy-2-[[1-(phenylmethyl)-4-piperidinyl]methyl]- (9CI) (CA INDEX NAME)



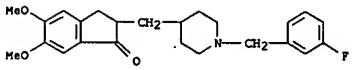
RN 120014-09-7 HCAPLUS
CN 1H-Inden-1-one, 5,6-diethoxy-2,3-dihydro-2-[[1-(phenylmethyl)-4-piperidinyl]methyl]- (9CI) (CA INDEX NAME)



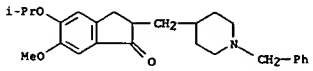
RN 120014-11-1 HCAPLUS
CN 1H-Inden-1-one, 2,3-dihydro-5,6-dimethoxy-2-{[1-[(3-nitrophenyl)methyl]-4-piperidinyl]methyl}- (9CI) (CA INDEX NAME)



RN 120014-13-3 HCAPLUS
CN 1H-Inden-1-one, 2-[[1-[(3-fluorophenyl)methyl]-4-piperidinyl]methyl]-2,3-dihydro-5,6-dimethoxy- (9CI) (CA INDEX NAME)

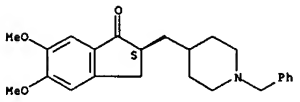


RN 120014-15-5 HCAPLUS
CN 1H-Inden-1-one, 2,3-dihydro-6-methoxy-5-(1-methylethoxy)-2-[[1-(phenylmethyl)-4-piperidinyl]methyl]- (9CI) (CA INDEX NAME)



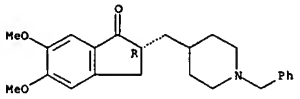
RN 142057-80-5 HCAPLUS
CN 1H-Inden-1-one, 2,3-dihydro-5,6-dimethoxy-2-[[1-(phenylmethyl)-4-piperidinyl]methyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 142698-19-9 HCAPLUS
CN 1H-Inden-1-one, 2,3-dihydro-5,6-dimethoxy-2-[[1-(phenylmethyl)-4-piperidinyl]methyl]-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

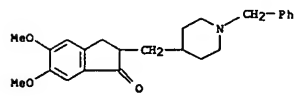


L5 ANSWER 16 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:56700 HCAPLUS
DOCUMENT NUMBER: 141:150902
TITLE: Human liver aldehyde oxidase: inhibition by 239 drugs
AUTHOR(S): Obach, R. Scott; Huynh, Phuong; Allen, Mary C.; Beedham, Christine
CORPORATE SOURCE: Groton Laboratories, Pfizer Global Research and Development, Groton, CT, USA
SOURCE: Journal of Clinical Pharmacology (2004), 44(1), 7-19
CODEN: JCPCBR; ISSN: 0091-2700
PUBLISHER: Sage Publications
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors tested 239 frequently used drugs and other compds. for their potential to inhibit the drug-metabolizing enzyme, aldehyde oxidase, in human liver cytosol. A sensitive, moderate throughput HPLC-MS assay was developed for 1-phthalazinone, the aldehyde oxidase-catalyzed product of phthalazine oxidation Inhibition of this activity was examined for the 239 drugs and other compds. of interest at a test concentration of 50 μM. Thirty-six compds. exhibited greater than 80% inhibition and were further examined for measurement of IC50. The most potent inhibitor observed was the selective estrogen receptor modulator, raloxifene (IC50 = 2.9 nM), and tamoxifen, estradiol, and ethinyl estradiol were also potent inhibitors. Other classes of drugs that demonstrated inhibition of aldehyde oxidase included phenothiazines, tricyclic antidepressants, tricyclic atypical antipsychotic agents, and dihydropyridine calcium channel blockers, along with some other drugs, including loratadine, cyclobenzaprine, amodiaquine, maprotiline, ondansetron, propafenone, domperidone, quinacrine, ketoconazole, verapamil, tacrine, and salmeterol. These findings are discussed in context to potential drug interactions that could be observed between these agents and drugs for which aldehyde oxidase is involved in metabolism and warrant investigation of the possibility of clin. drug interactions mediated by inhibition of this enzyme.

IT 120014-06-4, Donepezil
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cognitive enhancer donepezil ineffective in inhibition of human liver aldehyde oxidase)

RN 120014-06-4 HCAPLUS
CN 1H-Inden-1-one, 2,3-dihydro-5,6-dimethoxy-2-[[1-(phenylmethyl)-4-piperidinyl]methyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 17 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:907186 HCAPLUS
DOCUMENT NUMBER: 138:350
TITLE: Agents and crystals for improving excretory potency of urinary bladder
INVENTOR(S): Ishihara, Yuji; Doi, Takayuki; Nagabukuro, Hiroshi; Ishichi, Yuji
PATENT ASSIGNEE(S): Japan
SOURCE: U.S. Pat. Appl. Publ., 65 pp., Cont.-in-part of U. S. Ser. No. 787,288.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002177593	A1	20021128	US 2001-960477	20010924
JP 2003192593	A2	20030709	JP 2002-354856	19990929
JP 2003201237	A2	20030718	JP 2002-354833	19990929
JP 3512786	B2	20040331		
WO 2000018391	A1	20000406	WO 1999-JP5367	19990930
W: AE, AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CR, CU, CZ, DM, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, US, UZ, VN, YU, ZA				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1604653	A1	20051214	EP 2005-20329	19990930
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
CN 1768745	A	20060510	CN 2005-10118165	19990930
JP 2001335576	A2	20011204	JP 2001-85190	20010323
PRIORITY APPLN. INFO.:			JP 1998-276677	A 19980930
			WO 1999-JP5367	W 19990930
			US 2001-787288	A2 20010315
			JP 2001-85190	A 20010323
			JP 1999-275614	A3 19990929
			CN 2004-10039684	A3 19990930
			EP 1999-969675	A3 19990930
			JP 2000-88523	A 20000324

parent

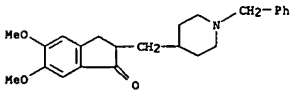
OTHER SOURCE(S): MARPAT 138:350

AB Agents for improving potency of the urinary bladder which comprises an amine compound of non-carbamate-type having an acetylcholinesterase-inhibiting action. Particularly, crystals of a tricyclic, condensed, heterocyclic derivative are provided, which possess an excellent action to inhibit acetylcholinesterase and an action to improve the excretory potency of urinary bladder. As an example, crystals of 8-[3-[1-[(3-fluorophenyl)-methyl]-4-piperidinyl]-1-oxopropyl]-1,2,5,6-tetrahydro-4H-pyrrolo[3,2,1-ij]quinolin-4-one or a salt thereof and pharmaceutical compns. containing them are disclosed.

IT 120011-70-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(agents and crystals for improving excretory potency of urinary bladder with acetylcholinesterase-inhibiting action)

RN 120011-70-3 HCAPLUS

L5 ANSWER 17 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)
CN 1H-Inden-1-one, 2,3-dihydro-5,6-dimethoxy-2-[[1-(phenylmethyl)-4-piperidinyl]methyl]-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

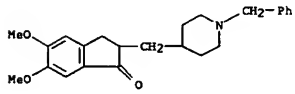
L5 ANSWER 18 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:623231 HCAPLUS
DOCUMENT NUMBER: 137:179283
TITLE: The tolerability and safety of cholinesterase inhibitors in the treatment of dementia
AUTHOR(S): Inglis, F.
CORPORATE SOURCE: Glasgow Memory Clinic, Clydebank, UK
SOURCE: International Journal of Clinical Practice, Supplement (2002), 127, 45-63
CODEN: ICPSFY; ISSN: 1368-504X
PUBLISHER: Medicom International
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Cholinesterase inhibitors (ChEIs) are dosed in two phases for the treatment of dementia, an initial dose-escalation phase to achieve a therapeutic dose and a maintenance phase where the therapeutic dose is given for long-term therapy. ChEIs are associated with a range of side effects as a result of cholinergic stimulation in different areas of the brain and the periphery. Acute, centrally-mediated gastrointestinal events (mostly nausea and vomiting) are class effects of all ChEIs, and are reported mostly during the dose-escalation phase of therapy. These events have been associated more with the dual acetylcholinesterase/butyrylch olinesterase (AChE/BuChE) inhibitor rivastigmine than with the AChE-selective inhibitors donepezil and galantamine, probably due to rivastigmine's higher potency. However, these events can be minimized using slow dose escalation with small dose graduations and administration with food. Other side effects associated with ChEIs include central nervous system events, extrapyramidal symptoms, sleep disturbances and cardiorespiratory events, associated with cholinergic activity in the cortex, caudate nucleus, brainstem and medulla, resp., and muscle cramps and weakness, cardiorespiratory events and urinary incontinence, associated with peripheral cholinergic activity. These symptoms are mostly reported during the maintenance phase of therapy. They are more frequently reported with donepezil, but are rarely reported with rivastigmine, and galantamine may not have been marketed long enough to make an adequate assessment. These differences are due to the drugs' resp. pharmacol. For example, donepezil and rivastigmine are active centrally, in contrast to galantamine, which is more active peripherally. Furthermore, rivastigmine preferentially inhibits the G1 isoform of cholinesterase, predominantly located in the cortex, hippocampus and in neuritic plaques, while donepezil and galantamine are not selective for any cholinesterase isoforms and have wide cholinergic activity both centrally and peripherally. The cholinergic activity of rivastigmine, in contrast to donepezil and galantamine, is apparently more targeted at clin. relevant brain sites. The pharmacol. profile of rivastigmine results in it having a low potential to interact with other drugs and it may be used with a high margin of safety in patients having a wide variety of concomitant diseases. Donepezil and galantamine may have significant interactions with other drugs that are metabolized by the hepatic cytochrome system and therefore need to be used with caution in patients with many concomitant illnesses. When dosed with care, ChEIs are well tolerated and patient compliance and patient and caregiver acceptability are good. The favorable tolerability and safety profiles of these agents make them suitable first-line therapy for dementia. In addition, patients who have tolerability and/or safety problems in maintenance treatment that

L5 ANSWER 18 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)
limit the use of donepezil or galantamine may benefit from switching to rivastigmine.

IT 120014-06-4, Donepezil
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tolerability and safety of cholinesterase inhibitors in treatment of dementia)

RN 120014-06-4 HCAPLUS
CN 1H-Inden-1-one, 2,3-dihydro-5,6-dimethoxy-2-[[1-(phenylmethyl)-4-piperidinyl]methyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 129 THERE ARE 129 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 19 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:816459 HCAPLUS
DOCUMENT NUMBER: 135:339302
TITLE: Methods and compositions for enhancing cellular function through protection of tissue components
INVENTOR(S): Frey, William H., II; Fawcett, John Randall; Thorne, Robert Gary; Chen, Xueqing
PATENT ASSIGNEE(S): Healthpartners Research Foundation, USA
SOURCE: PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001082932	A2	20011108	WO 2001-US13931	20010430
WO 2001082932	A3	20020718		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002028786	A1	20020307	US 2001-844450	20010427
US 7084126	B2	20060801		
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EP 1278525	A2	20030129	EP 2001-930957	20010430
EP 1278525	B1	20061102		
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US 2005272642	A1	20051208	US 2005-191901	20050728
US 2006009413	A1	20060112	US 2005-220115	20050906
US 2006009414	A1	20060112	US 2005-220116	20050906
US 2006014716	A1	20060119	US 2005-220223	20050906
US 2006030542	A1	20060209	US 2005-220222	20050906
PRIORITY APPLN. INFO.:			US 2000-200843P	P 20000501
			US 2000-230263P	P 20000906
			US 2000-233025P	P 20000915
			US 2001-844450	A3 20010427
			WO 2001-US13931	W 20010430

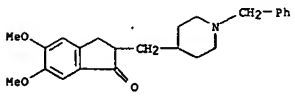
OTHER SOURCE(S): MARPAT 135:339302

AB Methods and compns. for enhancing cellular function through protection of tissue components, such as receptors, proteins, lipids, nucleic acids, carbohydrates, hormones, vitamins, and cofactors, by administering pyrophosphate analogs or related compds. Preferably, the invention provides a method for protecting a muscarinic acetylcholine receptor (mAChR) an/or increasing the efficacy of and agent the directly or indirectly affects a mAChR in a subject in need thereof.

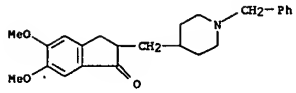
IT 120014-06-4, Donepezil
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering pyrophosphate analogs and combination with other agents)

RN 120014-06-4 HCAPLUS

L5 ANSWER 19 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)
CN 1H-Inden-1-one, 2,3-dihydro-5,6-dimethoxy-2-[[1-(phenylmethyl)-4-piperidinyl]methyl]- (9CI) (CA INDEX NAME)



L5 ANSWER 20 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



● HCl

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 20 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:586233 HCAPLUS
DOCUMENT NUMBER: 136:165284
TITLE: Actigraphic sleep-wake patterns and urinary 6-sulfatoxymelatonin excretion in patients with Alzheimer's disease
AUTHOR(S): Luboshitzky, Rafael; Shen-Orr, Zilla; Tzischichinksy, Orna; Maldonado, Marina; Herer, Paula; Lavie, Peretz
CORPORATE SOURCE: Haemek Medical Center, Endocrine Institute, Afula, 18101, Israel
SOURCE: Chronobiology International (2001), 18(3), 513-524
CODEN: CHBIE4; ISSN: 0742-0528
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Recent studies suggest melatonin, due to its antioxidant and free-radical-scavenging actions, may play a role in the neuroprotection against amyloid, which is implicated in the pathogenesis of Alzheimer's disease (AD). In this study, the authors determined urinary 6-sulfatoxymelatonin (aMT6s) excretion together with actigraphic sleep-wake patterns of untreated male patients with AD who lived at home. Results were compared with those obtained from normal age-matched elderly and normal young male subjects. Similar measurements were also performed in another group of patients with AD who were treated with a cholinesterase inhibitor (Donepezil, Aricept). Total 24h aMT6s values were significantly reduced in elderly controls (19.9h ± 5.2 μg/24h), in those with untreated AD (12.7 ± 4.4 μg/24h), and in patients treated for AD (12.4 ± 4.4 μg/24h) compared with normal young men (32.8 ± 3.1 μg/24h). A day-night difference in aMT6s was evident in all young controls, in 50% of elderly controls, in only 20% of patients with untreated AD, and in 67% of those with AD receiving Aricept. Sleep quality (expressed as sleep efficiency, wake time, and long undisturbed sleep duration) was better in young and elderly controls compared with the 2 groups of patients with AD. There was no significant correlation between aMT6s values or sleep patterns and the severity of cognitive impairment in patients with AD. Taken together, these data suggest that disrupted sleep, decreased melatonin production, and partial lack of day-night difference in melatonin secretion were observed equally in normal elderly and in patients with AD. Our results do not permit drawing any conclusion as to whether changes in urinary aMT6s excretion is correlated with disturbed sleep in patients with AD.

IT 120011-70-3, Aricept
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aricept effect on sleep-wake patterns and urinary 6-sulfatoxymelatonin excretion in patients with Alzheimer's disease)

RN 120011-70-3 HCAPLUS
CN 1H-Inden-1-one, 2,3-dihydro-5,6-dimethoxy-2-[[1-(phenylmethyl)-4-piperidinyl]methyl]-, hydrochloride (9CI) (CA INDEX NAME)

L5 ANSWER 21 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:608551 HCAPLUS
DOCUMENT NUMBER: 133:213151
TITLE: Pharmaceutical compositions and methods for improved delivery of hydrophobic therapeutic agents
INVENTOR(S): Patel, Manesh V.; Chen, Feng-Jing
PATENT ASSIGNEE(S): Lipocine, Inc., USA
SOURCE: PCT Int. Appl., 98 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 13
PATENT INFORMATION:

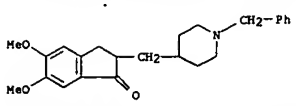
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000050007	A1	20000831	WO 2000-US165	20000105
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6294192	B1	20010925	US 1999-258654	19990226
CA 2365536	AA	20000831	CA 2000-2365536	20000105
AU 2000022242	A5	20000914	AU 2000-22242	20000105
AU 771659	B2	20040401		
EP 1158959	A1	20011205	EP 2000-901394	20000105
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002537317	T2	20021105	JP 2000-600619	20000105
NZ 513810	A	20040227	NZ 2000-513810	20000105
PRIORITY APPLN. INFO.:			US 1999-258654 A	19990226
			WO 2000-US165 W	20000105

AB The present invention relates to triglyceride-free pharmaceutical compns. for delivery of hydrophobic therapeutic agents. Compns. of the present invention include a hydrophobic therapeutic agent and a carrier, where the carrier is formed from a combination of a hydrophilic surfactant and a hydrophobic surfactant. Upon dilution with an aqueous solvent, the composition forms a clear, aqueous dispersion of the surfactants containing the therapeutic agent.
The invention also provides methods of treatment with hydrophobic therapeutic agents using these compns. A pharmaceutical composition contained cyclosporin 0.14, Cremophor RH-40 0.41, Arlacel186 0.29, sodium taurocholate 0.26, and propylene glycol 0.46 mg.

IT 120014-06-4, Donepezil
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compns. and methods for improved delivery of hydrophobic therapeutic agents)

RN 120014-06-4 HCAPLUS
CN 1H-Inden-1-one, 2,3-dihydro-5,6-dimethoxy-2-[[1-(phenylmethyl)-4-piperidinyl]methyl]- (9CI) (CA INDEX NAME)

L5 ANSWER 21 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



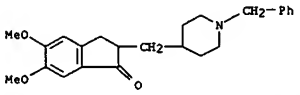
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 22 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:604488 HCAPLUS
DOCUMENT NUMBER: 134:141630
TITLE: Urinary incontinence: an unrecognized adverse effect with donepezil
AUTHOR(S): Hashimoto, M.; Imamura, T.; Tanimukai, S.; Kazui, H.; Mori, E.
CORPORATE SOURCE: Departments of Clinical Neurosciences, Hyogo Institute for Aging Brain and Cognitive Disorders, Himeji, 670-0981, Japan
SOURCE: Lancet (2000), 356(9229), 568
CODEN: LANCAO; ISSN: 0140-6736
PUBLISHER: Lancet Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Donepezil has been licensed since 1999 for use in Japan to improve cognitive function. Among 94 patients with probable Alzheimer's disease who were treated with donepezil, seven developed urinary incontinence, although this event was transient in most patients.

IT 120014-06-4, Donepezil
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(urinary incontinence as adverse effect of donepezil in humans with Alzheimer's disease)

RN 120014-06-4 HCAPLUS
CN 1H-Inden-1-one, 2,3-dihydro-5,6-dimethoxy-2-[[1-(phenylmethyl)-4-piperidinyl]methyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 23 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:227495 HCAPLUS
DOCUMENT NUMBER: 132:260683
TITLE: Acetylcholinesterase-inhibiting amines for improving bladder vesical excretory strength
INVENTOR(S): Ishihara, Yuji; Doi, Takayuki; Nagabukuro, Hiroshi; Ishichi, Yuji
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 165 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000018391	A1	20000406	WO 1999-JP5367	19990930
W: AE, AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CR, CU, CZ, DM, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, US, UZ, VN, YU, ZA				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
JP 2000169373	A2	20000620	JP 1999-275614	19990929
JP 2003192593	A2	20030709	JP 2002-354856	19990929
JP 2003201237	A2	20030718	JP 2002-354833	19990929
JP 3512786	B2	20040331		
CA 2344894	AA	20000406	CA 1999-2344894	19990930
AU 9959995	A1	20000417	AU 1999-59995	19990930
AU 758802	B2	20030327		
EP 1118322	A1	20010725	EP 1999-969675	19990930
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BR 9914163	A	20010814	BR 1999-14163	19990930
HU 200104493	A2	20020429	HU 2001-4493	19990930
NZ 510685	A	20031031	NZ 1999-510685	19990930
CN 1535682	A	20041013	CN 2004-10039684	19990930
CN 1572299	A	20050202	CN 2004-10062846	19990930
EP 1604653	A1	20051214	EP 2005-20329	19990930
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CN 1768745	A	20060510	CN 2005-10118165	19990930
ZA 2001002426	A	20010925	ZA 2001-2426	20010323
NO 2001001602	A	20010522	NO 2001-1602	20010329
US 2002177593	A1	20021128	US 2001-960477	20010924
US 2004116457	A1	20040617	US 2003-726486	20031204

PRIORITY APPLN. INFO.:

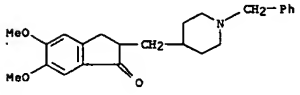
JP 1998-276677	A	19980930
JP 1999-275614	A3	19990929
CN 2004-10039684	A3	19990930
EP 1999-969675	A3	19990930
WO 1999-JP5367	W	19990930
US 2001-787288	A2	20010315
JP 2001-85190	A	20010323

OTHER SOURCE(S): MARPAT 132:260683

AB Drugs for improving bladder vesical excretory strength which contain a non-carbamate amine compound (Markush's structures given) having an acetylcholinesterase inhibitory effect.

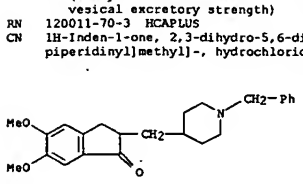
IT 120014-06-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(acetylcholinesterase-inhibiting amines for improving bladder vesical excretory strength)

RN 120014-06-4 HCAPLUS
CN 1H-Inden-1-one, 2,3-dihydro-5,6-dimethoxy-2-[[1-(phenylmethyl)-4-piperidinyl]methyl]- (9CI) (CA INDEX NAME)



IT 120011-70-3
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(acetylcholinesterase-inhibiting amines for improving bladder vesical excretory strength)

RN 120011-70-3 HCAPLUS
CN 1H-Inden-1-one, 2,3-dihydro-5,6-dimethoxy-2-[[1-(phenylmethyl)-4-piperidinyl]methyl]-, hydrochloride (9CI) (CA INDEX NAME)



REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

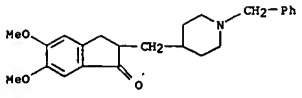
L5 ANSWER 24 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:778683 HCAPLUS
DOCUMENT NUMBER: 132:87724
TITLE: Absorption, distribution, metabolism, and excretion of donepezil (aricept) after a single oral administration to rat
AUTHOR(S): Matsui, Kenji; Mishima, Mannen; Nagai, Yasushi; Yuzuriha, Teruaki; Yoshimura, Tsutomu
CORPORATE SOURCE: Drug Dynamics Research Section, Drug Safety and Disposition Research Laboratories, Eisai Co., Ltd., Ibaraki, 300-2635, Japan
SOURCE: Drug Metabolism and Disposition (1999), 27(12), 1406-1414
CODEN: DMDSAI; ISSN: 0090-9556
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Donepezil hydrochloride (Aricept) is a drug for the treatment of Alzheimer's disease. The absorption, distribution, metabolism, and excretion of donepezil were investigated in male Sprague-Dawley rats after a single oral administration. Orally administered 14C-labeled donepezil was absorbed rapidly. The plasma level of unchanged donepezil declined more rapidly than that of radioactivity, and the brain level of radioactivity declined almost in parallel with the plasma level of unchanged donepezil. The ratio of donepezil to total radioactivity in brain was 86.9 to 93.0%, indicating low permeability of the metabolites through the blood-brain barrier. No heterogeneous localization of radioactivity was recognized in the brain and the concentration in each part of the brain was 1.74 to 2.24 times the plasma concentration Cumulative biliary, urinary, and fecal excretion of radioactivity in bile duct-cannulated rats was 72.9, 24.4, and 8.84%, resp., of the administered radioactivity at 48 h after administration. These results indicate that the absorption of donepezil is almost complete, and that its metabolites are mainly excreted into feces through the bile and some of them are subject to enterohepatic circulation. The metabolism of donepezil was extensive in rats and involved O-demethylation, aromatic hydroxylation, N-dealkylation, N-oxidation, and glucuronide conjugation of O-demethylate. The structures of the metabolites were determined by mass spectrometry and 1H-NMR anal. In plasma, urine, and bile, O-glucuronides accounted for the majority of the radioactivity, and in brain, unchanged donepezil was mostly detected. No metabolites were found in brain. There was no notable accumulation of radioactivity in whole blood and tissues.

IT 120014-06-4, Donepezil
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(absorption, distribution, metabolism, and excretion of donepezil after a single oral administration to rat)

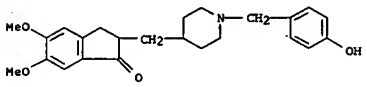
RN 120014-06-4 HCAPLUS
CN 1H-Inden-1-one, 2,3-dihydro-5,6-dimethoxy-2-[[1-(phenylmethyl)-4-piperidinyl]methyl]- (9CI) (CA INDEX NAME)

L5 ANSWER 24 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



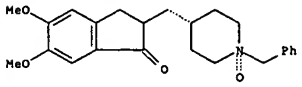
IT 142641-83-6 147427-77-8 147427-78-9
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(absorption, distribution, metabolism, and excretion of donepezil after a single oral administration to rat)

RN 142641-83-6 HCAPLUS
CN 1H-Inden-1-one, 2,3-dihydro-2-[[1-[(4-hydroxyphenyl)methyl]-4-piperidinyl]methyl]-5,6-dimethoxy- (9CI) (CA INDEX NAME)



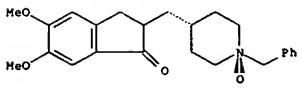
RN 147427-77-8 HCAPLUS
CN 1H-Inden-1-one, 2,3-dihydro-5,6-dimethoxy-2-[[cis-1-oxido-1-(phenylmethyl)-4-piperidinyl]methyl]- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 147427-78-9 HCAPLUS
CN 1H-Inden-1-one, 2,3-dihydro-5,6-dimethoxy-2-[[trans-1-oxido-1-(phenylmethyl)-4-piperidinyl]methyl]- (9CI) (CA INDEX NAME)

Relative stereochemistry.



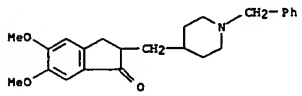
L5 ANSWER 24 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 25 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:748473 HCAPLUS
DOCUMENT NUMBER: 130:133615
TITLE: Tissue distribution of 14C-donepezil hydrochloride after a single oral administration to male rats by autoradiography
AUTHOR(S): Matsui, Kenji; Tadano, Kyoichi; Yoshimura, Tsutomu; Ueda, Masataka; Yuzuriha, Teruaki
CORPORATE SOURCE: Tsukuba Research Laboratories, Eisai Co., Ltd., Ibaraki-ken, Japan
SOURCE: Yakuri to Chiryo (1998), 26(Suppl. 6), S1373-S1378
CODEN: YACHDS; ISSN: 0386-3603
PUBLISHER: Raifu Saiensu Shuppan K.K.
DOCUMENT TYPE: Journal
LANGUAGE: Japanese

AB The tissue distribution of radioactivity in male rats has been studied using the technique of whole body autoradiog. following a single oral administration of 14C-donepezil hydrochloride, in aqueous solution at a nominal dose level of 1 mg/kg. At 0.5 h after dosing radioactivity was found mainly in the liver, gastrointestinal tract and organs associated with urinary excretion, with lower levels of radioactivity being found in the remaining tissues. Only low levels of radioactivity were found in the central nervous system with the pituitary gland and pineal body having slightly higher concns. of radioactivity than the rest of the central nervous system. At 24 h after dosing radioactivity was mainly associated with the gastrointestinal tract and concns. of radioactivity had declined in the remaining tissues. By 168 h after dosing, levels of radioactivity were too low for the distribution to be determined

IT 120011-70-3, Donepezil hydrochloride
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(tissue distribution of 14C-donepezil hydrochloride after a single oral administration to male rats by autoradiog.)

RN 120011-70-3 HCAPLUS
CN 1H-Inden-1-one, 2,3-dihydro-5,6-dimethoxy-2-[[1-(phenylmethyl)-4-piperidinyl]methyl]-, hydrochloride (9CI) (CA INDEX NAME)



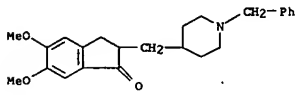
● HCl

L5 ANSWER 26 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:748431 HCAPLUS
DOCUMENT NUMBER: 130:148194
TITLE: Absorption, distribution, metabolism and excretion of 14C-donepezil hydrochloride after a single oral administration to beagle dogs
AUTHOR(S): Matsui, Kenji; Mizuo, Hitoshi; Mishima, Mannen; Tadano, Kyoichi; Yoshimura, Tsutomu; Yuzuriha, Teruaki; Sato, Tadashi
CORPORATE SOURCE: Tsukuba Research laboratories, Eisai Co., Ltd., Ibaraki-ken, Japan
SOURCE: Yakuri to Chiryo (1998), 26(Suppl. 6), S1357-S1371
CODEN: YACHDS; ISSN: 0386-3603
PUBLISHER: Raifu Saiensu Shuppan K.K.
DOCUMENT TYPE: Journal
LANGUAGE: Japanese

AB Single doses of 14C-donepezil hydrochloride were orally administered to beagle dogs to investigate its absorption, distribution, metabolism, and excretion. Orally administered 14C-donepezil hydrochloride was absorbed rapidly. The mean blood levels of radioactivity reached a peak (119±6.12 ng eq./mL) at 1.5 h after administration, and then declined polyexponentially. The tmax, Cmax, AUC(0-∞) and apparent t1/2 for the terminal phase was 1.5-2.0 h, 123±7.00 ng eq./mL, 2166±124 ng eq·hr/mL and 90.7±16.0 h, resp. The plasma levels of radioactivity were 1.03-2.03 fold higher than blood levels. The mean plasma levels of donepezil reached a peak (5.23±0.74 ng/mL) at 1.5 h after administration, and then declined biexponentially. The tmax, Cmax, AUG(0-6hr) and apparent t1/2 for the terminal phase in dogs was 1.5-2.0 h, 5.46±0.56 ng/mL, 20.4±2.77 ng·hr/mL and 3.65±0.96 h, resp. The AUC(0-6hr) of the unchanged donepezil accounted for 2.78% of the AUG(0-6hr) for total radioactivity. At 1.5 h after administration, which is the tmax of plasma radioactivity: excluding gastrointestinal tissues as the administration site, the highest concentration of radioactivity was found in the bile, the gallbladder and urine in urinary bladder. These were 747-106 times higher than the plasma concentration Almost all other tissues contained higher levels of radioactivity than plasma. In brain as the target organ: except for the hypophysis the concentration in each part of the brain was similar and 1.57-1.26 times higher than the plasma concentration At this time point, brain, liver and kidneys contained 0.26±0.06%, 22.4±2.68% and 1.10±0.35% of the administered radioactivity, resp. By 48 h after administration, the mean plasma level of radioactivity had decreased, however the levels in some tissues (e.g. ciliary body, choroidea, sclera) at this time were higher than these at 1.5 h. High concns. of radioactivity were detected in the bile, gallbladder, ciliary body, choroidea, iris, liver, urine in urinary bladder and sclera where the radioactive concns. were 2724-18.1 times higher than the plasma concentration By 168 h after administration, the mean plasma level of radioactivity decreased to 2.58±0.33 ng eu./mL, which is 1.17% of the maximum level. The radioactivity of all tissues except pigmented components in the eye declined at similar rate to that of the plasma levels of radioactivity. The concentration in other tissues had decreased to <5.02% of the maximum levels.
The main metabolites after oral administration of 14C-donepezil hydrochloride to the beagle dog were O-glucuronides of demethylated metabolites and N-dealkylated metabolite. Large amts. of deconjugated metabolites were found in the feces. Most of the radioactivity (80.8%) in the brain was found as the unchanged donepezil, indicating low permeability of metabolites through the blood-brain barrier. During the 24 h period after administration, 74.3±2.56% of the administered radioactive dose was recovered in the excreta, of which 17.8±1.63% was in urine and 56.5±3.78% in feces. During the 168 h period after administration, 98.3±0.87% of the administered radioactive dose was excreted, of which 21.4±1.71% was un urine and 77.1±1.10% in feces. The plasma protein binding of total radioactivity at 1.5 h after administration was 57.5±1.03%.

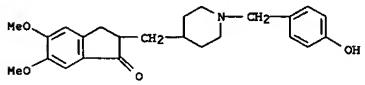
IT 120011-70-3, Donepezil hydrochloride
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(absorption, distribution, metabolism and excretion of 14C-donepezil hydrochloride after a single oral administration to beagle dogs)

RN 120011-70-3 HCAPLUS
CN 1H-Inden-1-one, 2,3-dihydro-5,6-dimethoxy-2-[[1-(phenylmethyl)-4-piperidinyl]methyl]-, hydrochloride (9CI) (CA INDEX NAME)



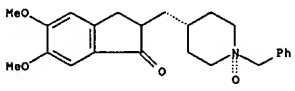
IT 142641-83-6 147427-77-8 147427-78-9
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(absorption, distribution, metabolism and excretion of 14C-donepezil hydrochloride after a single oral administration to beagle dogs)

RN 142641-83-6 HCAPLUS
CN 1H-Inden-1-one, 2,3-dihydro-2-[[1-[(4-hydroxyphenyl)methyl]-4-piperidinyl]methyl]-5,6-dimethoxy- (9CI) (CA INDEX NAME)



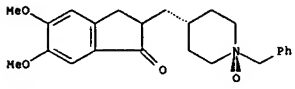
RN 147427-77-8 HCAPLUS
CN 1H-Inden-1-one, 2,3-dihydro-5,6-dimethoxy-2-[[cis-1-oxido-1-(phenylmethyl)-4-piperidinyl]methyl]- (9CI) (CA INDEX NAME)

L5 ANSWER 26 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)
Relative stereochemistry.



RN 147427-78-9 HCAPLUS
CN 1H-Inden-1-one, 2,3-dihydro-5,6-dimethoxy-2-[[trans-1-oxido-1-(phenylmethyl)-4-piperidinyl]methyl]- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L5 ANSWER 27 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:748419 HCAPLUS
DOCUMENT NUMBER: 130:148553
TITLE: Absorption, distribution, metabolism and excretion of 14C-donepezil hydrochloride after a single oral administration to rats
AUTHOR(S): Matsui, Kenji; Kagei, Yoshio; Mizuo, Hitoshi; Mishima, Mannen; Tadano, Kyoichi; Yoshimura, Tsutomu; Yuzuriha, Teruaki; Sato, Tadashi
CORPORATE SOURCE: Tsukuba Research Laboratories, Eisai Co., Ltd., Japan
SOURCE: Yakuri to Chiryo (1998), 26(Suppl. 6), S1339-S1355
CODEN: YACHDS; ISSN: 0386-3603
PUBLISHER: Raifu Saiensu Shuppan K.K.
DOCUMENT TYPE: Journal
LANGUAGE: Japanese

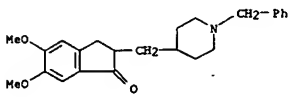
AB Single doses of 14C-donepezil hydrochloride were orally administered to rats to investigate its absorption, distribution, metabolism, and excretion. Orally administered 14C-donepezil hydrochloride was absorbed rapidly. In intact rats, the mean blood level of radioactivity reached a peak (61.1 ± 6.26 ng eq./mL, mean ± S.E.M.) at 30 min after administration, and then declined with 2 small peaks at 6 and 14 h. AUC(0-72h) was 1346 ± 66.8 ng·eq. h/mL. In bile duct-cannulated rats, the mean blood level of radioactivity reached a peak (107.3 ± 29.9 ng eq./mL) at 1.0 h after administration, and then declined. AUC(0-72h) was 657 ± 38.0 ng eq.·h/mL. The plasma levels of donepezil declined more rapidly than those of radioactivity. In contrast, brain levels of radioactivity declined in a manner similar to the brain levels of unchanged donepezil. The ratio of donepezil to total radioactivity in brain 0.5, 4, and 8 h after administration was 93.0%, 87.9%, and 86.9%, resp., indicating low permeability of metabolites through the blood-brain barrier. At 30 min after administration except for the gastrointestinal tissues at the site of administration, the highest concns. of radioactivity were found in the liver, pancreas, hypophysis, adrenals, kidneys, and bone marrow, which were 31.9-11.4 times higher than the plasma concentration Brain, liver, and kidneys contained 0.19 ± 0.05%, 14.0 ± 2.62%, and 1.48 ± 0.34% of the administrated radioactivity, resp. In brain as the target organ, radioactivity was measured sep. in the cerebrum, hypothalamus, hippocampus, striatum, cerebellum, and hypophysis. Except for the hypophysis, the concentration of radioactivity in each part of the brain was similar and 1.74-2.24 times higher than the plasma concentration At 168 h after administration, no radioactivity was detected in any tissues except for the testis and liver, in which the concns. were 0.93% and 0.06% of each of the maximum The main metabolites after oral administration of 14C-donepezil hydrochloride were glucuronide conjugates of demethylated metabolites and N-dealkylated metabolite. Large amts. of deconjugated metabolites were found in the feces. During the 24-h period after administration, 91.2 ± 0.71% of the administered dose was recovered in the excreta, of which 36.9 ± 0.81% was in urine and 54.3 ± 0.32% in feces. By 168 h after administration, 98.9 ± 0.77% of the administered dose was excreted, of which 39.2 ± 0.65% was in urine and 59.7 ± 0.64% in feces.
Cumulative biliary, urinary, and fecal excretion of radioactivity after a single oral dose of 14C-donepezil hydrochloride to bile duct-cannulated rats were determined In the bile, 70.1%, 72.2%, and 72.9% of administered radioactivity was excreted by 12, 24, and 48 h after administration, resp. In the urine and feces concurrently collected, 24.4% and 8.84% of the administered radioactivity was excreted by 48 h after administration, resp. These results indicate that the metabolites of donepezil are mainly excreted into feces through the bile. By 48 h, 97.3% of the administered radioactivity was recovered in the urine and

L5 ANSWER 27 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)
bile. Plasma protein binding of total radioactivity at 30 min and 4, 8, and 12 h after administration was 57.9 ± 1.55%, 59.0 ± 2.90%, 64.8 ± 2.61%, and 64.1 ± 0.69%, resp., with no changes in the binding depending on collection time.

IT 120011-70-3, Donepezil hydrochloride
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(absorption and distribution and metabolism and excretion of donepezil hydrochloride after single oral administration)

RN 120011-70-3 HCAPLUS

CN 1H-Inden-1-one, 2,3-dihydro-5,6-dimethoxy-2-[[1-(phenylmethyl)-4-piperidinyl]methyl]-, hydrochloride (9CI) (CA INDEX NAME)

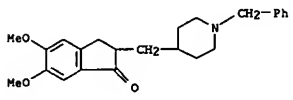


● HCl

IT 120011-70-3D, Donepezil hydrochloride, metabolites
RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(absorption and distribution and metabolism and excretion of donepezil hydrochloride after single oral administration)

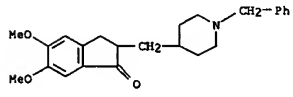
RN 120011-70-3 HCAPLUS

CN 1H-Inden-1-one, 2,3-dihydro-5,6-dimethoxy-2-[[1-(phenylmethyl)-4-piperidinyl]methyl]-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

L5 ANSWER 28 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



● HCl

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 28 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:747944 HCAPLUS
DOCUMENT NUMBER: 130:134062
TITLE: One-year oral toxicity study of donepezil hydrochloride in dogs
AUTHOR(S): Auletta, Carol S.; Mitchell, John M.; Richer, Ward R.; Noguchi, Masayoshi; Sagami, Fumiko
CORPORATE SOURCE: Huntingdon Life Sciences, Millstone, NJ, USA
SOURCE: Yakuri to Chiryo (1998), 26(Suppl. 6), S1197-S1225
CODEN: YACHDS; ISSN: 0386-3603
PUBLISHER: Raifu Saiensu Shuppan K.K.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB This study was designed to assess the potential toxicity of donepezil hydrochloride when administered orally, in gelatin capsules, to Beagle dogs (6 per sex per group) for up to 12 mo at doses of 0.6, 2, and 5 mg/kg of body weight per day. Control animals (6 per sex) received gelatin capsules containing 5 mg per kg of body weight per day of the carrier (α-lactose, hydroxypropyl cellulose). Two animals per sex per group were selected for interim necropsy after 6 mo of treatment. No chronic toxic effects occurred. There was no mortality attributed to donepezil hydrochloride. One control animal died of non-treatment-related causes during the second week of the study; all other animals survived to study termination. Treatment-related pharmacol. effects consistent with the action of this drug (cholinesterase inhibition) consisted of salivation in all dose groups and lacrimation and tremors and(or) hyperactivity in the mid- and high-dose groups (2 and 5 mg/kg/day). Possible pharmacol. effects consisted of slight decreases in water consumption, urine volume, and urinary electrolyte excretion in high-dose males and(or) females and slight decreases in urine volume and urinary electrolyte excretion in mid-dose males. Changes in food consumption were limited to slight decreases in the high-dose group during the first week only. Cmax and AUC clearly increased with increasing dosage, and these increases appeared to be more than dose-proportional. No sex differences in toxicokinetics were found in any dosage group. No treatment-related adverse effects were evident from body wts., ophthalmol. examns., clin. pathol. studies (hematol., clin. biochem., and protein electrophoresis), or postmortem evaluations (organ wts. and macroscopic examns).

IT 120011-70-3, Donepezil hydrochloride
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(toxicity of donepezil hydrochloride in dogs after oral administration)

RN 120011-70-3 HCAPLUS

CN 1H-Inden-1-one, 2,3-dihydro-5,6-dimethoxy-2-[[1-(phenylmethyl)-4-piperidinyl]methyl]-, hydrochloride (9CI) (CA INDEX NAME)

L5 ANSWER 29 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:747925 HCAPLUS
DOCUMENT NUMBER: 130:134061
TITLE: One-year oral toxicity study of donepezil hydrochloride in rats
AUTHOR(S): Auletta, Carol S.; Mitchell, John M.; Richer, Ward R.; Taki, Toyohiko; Sagami, Fumio
CORPORATE SOURCE: Huntingdon Life Sciences, Millstone, NJ, USA
SOURCE: Yakuri to Chiryo (1998), 26(Suppl. 6), S1177-S1195
CODEN: YACHDS; ISSN: 0386-3603
PUBLISHER: Raifu Saiensu Shuppan K.K.
DOCUMENT TYPE: Journal
LANGUAGE: English

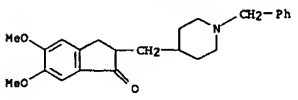
AB This study was designed to assess the potential toxicity of donepezil hydrochloride when administered orally, via oral gavage, to Sprague-Dawley rats (40 per sex per group) for up to 12 mo at doses of 1, 3, and 10 mg per kg of body weight per day. Control animals (40 per sex) received the vehicle (distilled water) at the same dose volume as administered to the treated animals. Five animals per sex per group were selected for pharmacokinetic anal. and 10 animals per sex per group were selected for interim necropsy after 6 mo of treatment. Expected pharmacol. effects were seen at all doses. The only toxic effect was a decrease in body weight gain in animals which received the highest dose (10 mg/kg/day). There was no mortality attributed to donepezil hydrochloride. Signs consistent with the pharmacol. action of this material (cholinesterase inhibition) consisted of miosis in all drug-treated groups and salivation (males and females) and fasciculation (females) in the group which received 10 mg/kg. Increased wts. of the salivary glands in this group, with no histopathol. changes, appeared to be associated with the increased salivation. Increases in urinary electrolyte concns. and total electrolyte excretion in some treated groups for 4 h post-dose but not at 4-24 h or in the combined 0-24-h values at month 3 was considered to be a pharmacol. resulting from cholinergic action of donepezil hydrochloride. Decreases in body weight gain occurred in animals which received 10 mg/kg/day. No effects on body wts. were evident in the groups which received 1 and 3 mg/kg/day. Plasma concns. approx. increased with dose-related manner and repeated administration in both sexes. Slightly higher plasma concns. were observed in females than in the males in each dosing group. No treatment-related adverse effects were evident from food consumption, ophthalmol. examns., clin. pathol. studies (hematol. and clin. biochem.), or postmortem evaluations (organ wts. and macroscopic and microscopic examns.). Based on these results, the no-toxic-effect dose for oral administration of donepezil hydrochloride to Sprague-Dawley rats for 1 yr was 3 mg/kg/day.

IT 120011-70-3, Donepezil hydrochloride
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(toxicity of donepezil hydrochloride after oral administration)

RN 120011-70-3 HCAPLUS

CN 1H-Inden-1-one, 2,3-dihydro-5,6-dimethoxy-2-[[1-(phenylmethyl)-4-piperidinyl]methyl]-, hydrochloride (9CI) (CA INDEX NAME)

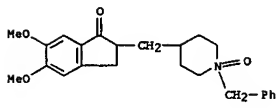
L5 ANSWER 29 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



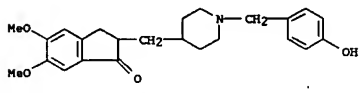
● HCl

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

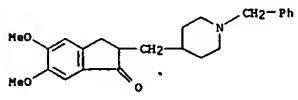
L5 ANSWER 30 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 142641-83-6 HCAPLUS
CN 1H-Inden-1-one, 2,3-dihydro-2-[[1-[(4-hydroxyphenyl)methyl]-4-piperidinyl]methyl]-5,6-dimethoxy- (9CI) (CA INDEX NAME)



IT 120011-70-3, E 2020
RL: BIOL (Biological study)
(metabolism and pharmacokinetics of oral, in human)
RN 120011-70-3 HCAPLUS
CN 1H-Inden-1-one, 2,3-dihydro-5,6-dimethoxy-2-[[1-(phenylmethyl)-4-piperidinyl]methyl]-, hydrochloride (9CI) (CA INDEX NAME)



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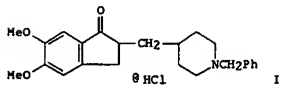
L5 ANSWER 30 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:573528 HCAPLUS
DOCUMENT NUMBER: 119:173528
TITLE: Pharmacokinetics of E2020, a new compound for Alzheimer's disease, in healthy male volunteers
AUTHOR(S): Mihara, M.; Ohnishi, A.; Tomono, Y.; Hasegawa, J.; Shimamura, Y.; Yamazaki, K.; Morishita, N.
CORPORATE SOURCE: Res. Dev. Div., Eisai Co., Ltd., Tokyo, 112-88, Japan
SOURCE: International Journal of Clinical Pharmacology, Therapy and Toxicology (1993), 31(5), 223-9
CODEN: IJCPB5; ISSN: 0300-9718
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB E2020 (I) is a new cholinesterase inhibitor with a novel chemical structure, which is under clin. investigation for use in Alzheimer's disease in Japan and the USA. Three sep. studies were conducted to evaluate the safety and to establish the pharmacokinetic profile of E2020 after oral administration to healthy male subjects. E2020 was administered as: (1) single oral doses (0.3 mg, 1 mg, 2 mg, 5 mg, 8 mg and 10 mg) in a fasting condition, (2) a single oral dose (2 mg) after a meal and (3) repeated oral doses (2 mg once daily for 21 days). The concns. of E2020 and its metabolites in plasma, serum, urine and feces were determined by HPLC methods with UV detection. E2020 was generally well tolerated by all subjects. In the single-dose study, there was a linear relationship between dose and mean AUC. The mean plasma half-life was about 50 h and was dose-independent. The total clearance and renal clearance of E2020 were also dose-independent and the mean values after 10 mg dosing were 9.7 L/h and 0.86 L/h, resp. The cumulative total urinary and fecal excretion of the sum of unchanged E2020 and its metabolites at 264 h after the administration of the single 10 mg dose was 36.1% and 8.6% of the dose, resp. The mean serum protein binding was 92.6%. No effect of food intake on the pharmacokinetics was observed Evaluation of the mean trough levels and AUC0-24 of E2020 indicated that a steady-state was achieved after approx. 2 wk of daily dosing.
IT 120013-84-5 142641-83-6
RL: BIOL (Biological study)
(as E 2020 metabolite, in feces and urine of human)
RN 120013-84-5 HCAPLUS
CN 1H-Inden-1-one, 2,3-dihydro-5,6-dimethoxy-2-[[1-oxido-1-(phenylmethyl)-4-piperidinyl]methyl]- (9CI) (CA INDEX NAME)